Search Strategy

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     FILE 'USPATFULL' ENTERED AT 17:08:36 ON 12 DEC 2002
                E PERRON HERVE/IN
L1            16 S E2-E3

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                E PERRON H/IN
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L3            37 S E3 OR E4 OR E7

     FILE 'USPATFULL' ENTERED AT 17:33:23 ON 12 DEC 2002
L4          8264 S MULTIPLE SCLEROSIS
L5          2239 S L4 AND (RETROVIR?)
L6           146 S L5 AND (RETROVIR?/CLM OR RETROVIR?/AB)
L7           121 S L6 AND (NUCLEIC ACID? OR DNA OR RNA OR CDNA OR MRNA)

     FILE 'WPIDS' ENTERED AT 17:35:19 ON 12 DEC 2002
L8          6333 S MULTIPLE SCLEROSIS
L9           143 S L8 AND RETROVIR?
L10           45 S L9 AND (NUCLEIC ACID?)

     FILE 'MEDLINE' ENTERED AT 17:35:45 ON 12 DEC 2002
L11        25449 S MULTIPLE SCLEROSIS
L12          215 S L11 AND RETROVIR?
L13           21 S L12 AND (CLONE? OR NUCLEIC ACID?)
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L1 ANSWER 1 OF 16 USPATFULL
2002:19207 Cell lines and viral isolates associated with multiple sclerosis.
Perron, Herve, Grenoble, FRANCE
Mallet, Francois, Villeurbanne, FRANCE
Mandrand, Bernard, Villeurbanne, FRANCE
Bedin, Frederic, Lyons, FRANCE
Beseme, Frederic, Villefontaine, FRANCE
Bio Merieux, Marcy l'Etoile, FRANCE (non-U.S. corporation)
US 6342383 B1 20020129
APPLICATION: US 1998-133411 19980813 (9)
PRIORITY: FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-1529 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition comprising two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of said virus, and a second agent, or a variant of said second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:
1. A continuous cell line designated LM7PC as deposited with the ECACC on Jan. 8, 1993 under Accession Number 93010817.

2. An isolated viral strain selected from the group consisting of: (a) a viral strain MS7PG deposited at the ECACC on Jan. 8, 1993 under Accession Number V93010816; (b) a viral strain obtained by culture of said viral strain MS7PG; (c) a viral strain obtainable from a cell line LM7PC, deposited at the ECACC on Jan. 8, 1993 under Accession Number 93010817; and (d) a viral strain from cells obtained by culture of said cell line LM7PC.

3. A continuous cell line obtained by culture of a viral strain of claim 2.

4. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain MS7PG.

5. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain obtained by culture of said viral strain MS7PG.

6. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain obtainable from said cell line LM7PC.

7. The isolated viral strain of claim 2, wherein said isolated viral strain is said viral strain from cells obtained by culture of said cell line LM7PC.

8. An isolated viral strain selected from the group consisting of: (a) a viral strain MS7PG deposited at the ECACC on Jan. 8, 1993 under Accession Number V93010816; and (b) a viral strain obtainable from a

cell line LM7PC, deposited at the ECACC on Jan. 8, 1993 under Accession Number 93010817.

L1 ANSWER 2 OF 16 USPATFULL
2001:158057 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6291225 B1 20010918
APPLICATION: US 1995-485145 19950607 (8)
PRIORITY: FR 1992-4322 19920403
FR 1992-13443 19921103
DOCUMENT TYPE: Utility; GRANTED.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Process for in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), according to which a body sample is taken from an individual suffering from MS, the sample is cultivated in a culture medium which promotes the growth of infected cells to obtain a culture of primary infected cells, and a sample of the culture of primary cells or of a subculture of the latter is cultivated in series, that is to say by successive passages, in the culture medium to obtain the culture or cell line infected by a virus associated with MS. The process includes a procedure in which the culture medium also contains a beta anti-interferon antibody or an antibody which is directed against an antigenically close molecule, the antibody playing an inhibiting role in viral expression and allowing long-lasting expression and propagation of the viral strain in the culture or cell line.

CLM What is claimed is:

1. A viral biological material selected from the group consisting of: (a) a viral strain POL-2 deposited at the ECACC on Jul. 22, 1992 under number V92072202; (b) a viral strain obtained by culture of said viral strain POL-2; (c) a viral strain obtainable from a cell line PLI-2, deposited at the ECACC on Jul. 22, 1992 under number 92072201; and (d) a viral strain from cells obtained by culture of said cell fine PLI-2.

2. The viral biological material of claim 1, wherein said viral biological material is being said viral strain POL-2 deposited at the ECACC on Jul. 22, 1992 under number V92072202.

3. The viral biological material of claim 1, wherein said viral biological material is said viral strain obtained by culture of said viral strain POL-2.

4. The viral biological material of claim 1, wherein said viral biological material is being said viral strain composition obtainable from said cell line PLI-2, deposited at the ECACC on Jul. 22, 1992 under number 92072201.

5. The viral biological material of claim 1, wherein said viral biological material is said viral strain from cells obtained by culture of said cell line PLI-2.

6. The viral biological material of claim 1, wherein said cell line PLI-2 is transfected by at least one immediate early gene of HSV-1 virus.

7. The viral biological material of claim 6, wherein said immediate early gene is selected from the group consisting of a gene which codes

for a protein ICPO of HSV-1 virus and a gene which codes for a protein ICP4 of HSV-1 virus.

8. A viral biological material selected from the group consisting of: (a) a viral strain POL-2 deposited at the ECACC on Jul. 22, 1992 under number V92072202 and (b) a viral strain obtainable from a cell line PLI-2, deposited at the ECACC on Jul. 22, 1992 under number 92072201.

L1 ANSWER 4 OF 16 USPATFULL
2001:18272 Viral isolates associated with multiple sclerosis.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyon, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6184025 B1 20010206
APPLICATION: US 1998-200990 19981130 (9)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition comprising two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of said virus, and a second agent, or a variant of said second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:
1. An isolated viral strain designated POL-2 as deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202, or designated MS7PG as deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, or any naturally occurring variant strains of said viral strains POL-2 and MS7PG.

2. A virus, in the purified or isolated state, possessing reverse transcriptase activity, associated with a family of endogenous retroviral elements and associated with multiple sclerosis, originating from a viral strain possessing reverse transcriptase activity, selected from the group consisting of a viral strain designated POL-2 as deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202, a viral strain designated MS7PG as deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816 and any naturally occurring variant strains of said viral strains POL-2 and MS7PG.

3. An isolated virus comprising a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9, their complementary sequences and their equivalent sequences, said equivalent sequences displaying, for any succession of 100 contiguous monomers, at least 50% identity with a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID

NO: 4, SEQ ID NO: 5, SEQ ID NO: 6; SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

4. An isolated retrovirus associated with multiple sclerosis, characterized in that the pol gene of its genome comprises an equivalent nucleotide sequence, said equivalent sequence displaying at least 50% identity with a nucleotide sequence belonging to the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

5. An isolated retrovirus associated with multiple sclerosis, characterized in that the pol gene of its genome codes for a peptide sequence displaying at least 50% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

6. An isolated retrovirus associated with multiple sclerosis, characterized in that the pol gene of its genome codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 50% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

7. The isolated virus according to claim 3, wherein said equivalent sequences display, for any succession of 100 contiguous monomers, at least 70% identity with a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

8. The retrovirus according to claim 4, wherein said equivalent nucleotide sequence displays at least 65% identity with nucleotide sequences belonging to the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

9. The retrovirus according to claim 5, wherein said pol gene coding for a peptide sequence displays at least 70% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

10. The retrovirus according to claim 5, characterized in that the pol gene of its genome codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 50% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

11. The retrovirus according to claim 10, wherein said pol gene codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 70% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

12. The retrovirus according to claim 6, wherein said pol gene codes for a peptide sequence displaying, for any contiguous succession of at least 30 amino acids, at least 70% identity with a peptide sequence encoded by a nucleotide sequence selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6,

SEQ ID NO: 7, SEQ ID NO: 8, SEQ ID NO: 9 and their complementary sequences.

13. The retrovirus according to claim 6, characterized in that the pol gene of its genome codes for a peptide sequence displaying at least 50% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

14. The retrovirus according to claim 13, wherein said pol gene codes for a peptide sequence displaying at least 70% identity with a peptide sequence encoded by the pol gene of the ERV-9 or HSERV-9 retrovirus genome.

L1 ANSWER 5 OF 16 USPATFULL
2000:70666 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 6071736 20000606
APPLICATION: US 1996-754010 19961120 (8)
PRIORITY: FR 1992-13443 19921103
FR 1993-9204322 19930403
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB In a process for the in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), a body sample is taken from an individual suffering from MS. The sample is cultivated in a culture medium that promotes the growth of infected cells to obtain a culture of primary infected cells. A sample of the culture of primary cells or a subculture of the latter is cultivated in series, by successive passages in the culture medium to obtain the culture or cell line infected by a virus associated with MS. The culture medium also contains a beta-interferon antibody or an antibody that is directed against an antigenically close molecule, the antibody playing an inhibiting role in viral expression and allowing long-lasting expression and propagation of the viral strain in the culture or cell line.
CLM What is claimed is:
1. A process for in vitro production of a culture or cell line infected by a viral strain, said viral strain having at least one of its replication and expression inhibited by a molecule which plays an inhibiting role in viral expression, said process comprising: obtaining a body sample from an individual infected with said viral strain, cultivating said body sample in a culture medium which promotes growth of infected cells to obtain a culture or cell line of primary infected cells, and cultivating by successive passages in said culture medium a sample of the culture or cell line of primary infected cells or a subculture of said culture or cell line to obtain the culture or cell line infected by said viral strain, wherein the culture medium also contains an antibody directed against said molecule which plays an inhibiting role in viral expression, and said culture medium allows persistent expression and propagation of the viral strain in the culture or cell line.

2. A culture medium for carrying out a process as claimed in claim 1, comprising at least one amino acid, at least one vitamin factor, at least one inorganic salt, glucose, and said antibody directed against said molecule which plays an inhibiting role in viral expression.

3. The culture medium according to claim 2, further comprising said viral strain.

4. The process according to claim 1, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon or a molecule antigenically close to beta-interferon.

5. The process according to claim 4, wherein said viral strain is associated with multiple sclerosis.

6. The process according to claim 1, wherein said viral strain is associated with multiple sclerosis.

7. The culture medium according to claim 2, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon or a molecule antigenically close to beta-interferon.

8. The culture medium according to claim 3, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon or a molecule antigenically close to beta-interferon.

9. The culture medium according to claim 3, wherein said viral strain is associated with multiple sclerosis.

10. The culture medium according to claim 8, wherein said viral strain is associated with multiple sclerosis.

11. The process according to claim 4, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon.

12. The culture medium according to claim 7, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon.

13. The culture medium according to claim 8, wherein said molecule which plays an inhibiting role in viral expression is beta-interferon.

L1 ANSWER 6 OF 16 USPATFULL
1999:163842 Isolated nucleotide sequences associated with Multiple sclerosis.
Perron, Herve, Lyons, France
Beseme, Frederic, Villefontaine, France
Bedin, Frederic, Lyons, France
Paranhos-Baccala, Glaucia, Lyons, France
Komurian-Pradel, Florence, Saint Cyr Au Mont D'or, France
Jolivet-Reynaud, Colette, Bron, France
Mandrand, Bernard, Villeurbanne, France
Bio Merieux, Marcy L'etoile, France (non-U.S. corporation)
US 6001987 19991214
APPLICATION: US 1996-691563 19960802 (8)
PRIORITY: FR 1995-9643 19950803
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Viral material, in the isolated or purified state, in which the genome comprises a nucleotide sequence chosen from the group including sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, their complementary sequences and their equivalent sequences, in particular nucleotide sequences displaying, for any succession of 100 contiguous monomers, at least 50% and preferably at least 70% homology with the said sequences SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53 and SEQ ID NO:56, respectively, and their complementary sequences.
CLM What is claimed is:

1. An isolated, purified or synthesized nucleotide sequence comprising a sequence selected from the group consisting of: SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61, SEQ ID NO:89, and a complementary sequence complementary to one of said SEQ ID NO:46, SEQ ID NO:51, SEQ ID NO:52, SEQ ID NO:53, SEQ ID NO:56, SEQ ID NO:58, SEQ ID NO:59, SEQ ID NO:60, SEQ ID NO:61 or SEQ ID NO:89.

L1 ANSWER 7 OF 16 USPATFULL
1999:121120 MSRV1 virus and MSRV2 pathogen and/or infective agent associated with multiple sclerosis, and biopolymer constituents thereof.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy I'Etoile, France (non-U.S. corporation)
US 5962217 19991005
APPLICATION: US 1995-470006 19950606 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:
1. An isolated or synthetic nucleotide fragment comprising a first nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, a fragment of SEQ ID NO:12 comprising at least 100 contiguous monomers of SEQ ID NO:12, and a complementary sequence complementary to one of said SEQ ID NO:10 through SEQ ID NO:15, SEQ ID NO:27 through SEQ ID NO:30, SEQ ID NO:34 through SEQ ID NO:37 or said fragment of SEQ ID NO:12.

2. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:10, or its complementary sequence.

3. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:11, or its complementary sequence.

4. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:12, a fragment of SEQ ID NO:12 comprising at least 100 contiguous monomers of SEQ ID NO:12 and a complementary sequence complementary to one of said SEQ ID NO:12 or said fragment of SEQ ID NO:12.

5. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:13, or its complementary sequence.

6. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:14, or its complementary sequence.

7. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:15, or its complementary sequence.

8. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:27, or its complementary sequence.

9. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:28, or its complementary sequence.

10. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:29, or its complementary sequence.

11. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:30, or its complementary sequence.

12. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:34, or its complementary sequence.

13. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:35, or its complementary sequence.

14. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:36, or its complementary sequence.

15. The nucleotide fragment according to claim 1, wherein said nucleotide sequence is SEQ ID NO:37, or its complementary sequence.

16. A specific primer for amplification by polymerization of a nucleic acid of a pathogenic or infectious agent associated with multiple sclerosis, said primer comprising at least six contiguous monomers of the nucleotide sequence of the nucleotide fragment according to claim 1.

17. The primer according to claim 16, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, and a complementary sequence complementary to one of said SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37.

18. A probe for specifically hybridizing with a nucleic acid of a pathogenic or infectious agent associated with multiple sclerosis, said probe comprising at least six contiguous monomers of the nucleotide sequence of the nucleotide fragment according to claim 1.

19. The probe according to claim 18, wherein said nucleotide sequence is selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, and a complementary sequence complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37.

20. A replication vector comprising the nucleotide fragment according to

claim 1 and a promoter sequence.

21. A diagnostic, composition comprising a nucleotide fragment according to claim 1.

22. An isolated pathogenic or infectious agent associated with multiple sclerosis, said agent having a genome comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, a fragment of SEQ ID NO:12 comprising at least 100 contiguous monomers of SEQ ID NO:12, and a complementary sequence complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12 or said fragment of SEQ ID NO:12.

23. The agent according to claim 22, said agent having a genome comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and a complementary sequence complementary to one of said SEQ ID NO:10, SEQ ID NO:1I or SEQ ID NO:12.

L1 ANSWER 8 OF 16 USPATFULL
1999:81747 Process for the production of a viable cell culture infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, L'Etoile, France (non-U.S. corporation)Universite Joseph Fourier (Grenoble 1), Grenoble Cedex, France (non-U.S. corporation)
US 5925555 19990720
APPLICATION: US 1996-651573 19960522 (8)
PRIORITY: FR 1992-4322 19920403
FR 1992-13447 19921103
DOCUMENT TYPE: Utility; Granted.

AB The present invention relates to a process for in vitro culture of cells infected by a virus associated with multiple sclerosis and to the infected cell lines thus produced. According to the invention, the process includes: a) cultivation of human cells infected by a viral strain to obtain at least one culture of primary cells infected by the viral strain, b) cultivation of non-infected human cells permissive to the viral strain to obtain at least one permissive culture, c) cocultivation of at least one sample of a culture of infected primary cells and one sample of the permissive culture to obtain a first infected derived culture, d) cultivation in series of the first infected derived culture. The invention is used in particular in the pharmaceutical diagnostics industry sector.

CLM What is claimed is:
1. A process for producing a viable infected culture or cell line comprising cells infected by at least one human viral strain associated with multiple sclerosis (MS) having reverse transcriptase activity, said process comprising: (a) cultivating cells infected by said viral strain to obtain at least one culture or cell line of primary cells infected by said viral strain, (b) cultivating non-infected leptomeningeal or plexus choroideus cells that are permissive to said viral strain to obtain at least one non-infected permissive culture, (c) cocultivating at least one sample of said culture or cell line of primary infected cells and at least one sample of said at least one non-infected permissive culture to obtain a first derived culture of leptomeningeal or plexus choroideus cells infected by said viral strain, and (d) cultivating the first infected derived culture in series, by cocultivating a new sample of the at least one non-infected permissive culture and a sample of the first infected derived culture, or of a subculture of the first infected derived culture, to obtain a new subculture of the first infected derived culture, constituting a viable viral culture or cell line.

2. The process as claimed in claim 1, wherein the culture or cell-line of infected primary cells is obtained from cells infected by said viral strain, said cells being selected from the group consisting leptomeningeal cells, plexus choroideus cells, myeloid blood cells and lymphocytes.

3. The process as claimed in claim 1, wherein the permissive culture is obtained from human plexus choroideus cells.

4. The process as claimed in claim 1, wherein several of said primary cultures infected by differing viral strains are obtained in step (a), and wherein step (c) is carried out by cocultivating a sample of the permissive culture and several differing samples of said infected primary cultures.

5. The process as claimed in claim 1, further comprising providing a culture medium for cultivating said permissive cells, wherein said culture medium comprises: between 400 and 2250 mg/l of amino acids; between 3.5 and 130 mg/l of vitamins; between 9100 and 13,000 mg/l of inorganic salts; and between 1000 and 6000 mg/l of glucose.

6. A viable cell culture infected by a human viral strain associated with multiple sclerosis, which comprises viable cells sampled from or belonging to a viable infected culture or cell line obtained by a process as claimed in claim 1, or viable derived cells obtained by modifying the genome of said cells, without altering their phenotype.

7. The process as claimed in claim 1, wherein the culture of infected primary cells is obtained from cells infected by said viral strain and selected from the group consisting of macrophages and monocytes.

8. The process as claimed in claim 5, wherein said culture medium further comprises at least one growth factor selected from the group consisting of endothelial cell growth factor and basic fibroblast growth factor.

9. The process as claimed in claim 1, wherein said at least one culture or cell line is an LM7-type culture or cell line.

10. A process for producing a viable infected culture or cell line comprising cells infected by at least one human viral strain associated with multiple sclerosis (MS) having reverse transcriptase activity, said process comprising: (a) cultivating cells infected by said viral strain and selected from the group consisting of leptomeningeal cells, plexus choroideus cells, myeloid blood cells and lymphocytes, to obtain at least one culture or cell line of primary cells infected by said viral strain, (b) cultivating plexus choroideus cells that are permissive to said viral strain to obtain at least one non-infected permissive culture, (c) cocultivating at least one sample of said culture or cell line of primary infected cells and at least one sample of said at least one non-infected permissive culture to obtain a first derived culture of plexus choroideus cells infected by said viral strain, and (d) cultivating the first infected derived culture in series, by cocultivating a new sample of the at least one non-infected permissive culture and a sample of the first infected derived culture or of a subculture of the first infected derived culture to obtain a new subculture of the first infected derived culture, constituting a viable viral culture or cell line.

11. The process as claimed in claim 10, wherein said human cells are

LM7-type cells.

12. A process for producing a viable infected culture or cell line comprising cells infected by multiple sclerosis (MS), said process comprising: (a) cultivating cells infected with MS to obtain at least one culture or cell line of primary infected cells, (b) cultivating non-infected leptomeningeal or plexus choroideus cells that are permissive to MS to obtain at least one non-infected permissive culture, (c) cocultivating at least one sample of said culture or cell line of primary infected cells and at least one sample of said at least one non-infected permissive culture to obtain a first infected derived culture, and (d) cultivating the first infected derived culture in series, by cocultivating a new sample of the at least one non-infected permissive culture and a sample of the first infected derived culture or of a subculture of the first infected derived culture to obtain a new subculture of the first infected derived culture, constituting a viable culture or cell line.

13. The process as claimed in claim 1, wherein said infected and non-infected cells are nervous system cells.

14. The process as claimed in claim 1, wherein the permissive culture is obtained from plexus choroideus cells.

15. The process as claimed in claim 1, wherein the infected and non-infected cells are human cells.

16. The process as claimed in claim 10, wherein the infected and non-infected cells are human cells.

L1 ANSWER 10 OF 16 USPATFULL
1999:21977 Retrovirus agents MSRV1 and MSRV2 associated with multiple sclerosis
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Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5871996 19990216
APPLICATION: US 1995-384137 19950206 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:

1. A composition comprising: a first agent comprising an isolated virus, wherein said virus possesses reverse transcriptase activity, and a second agent, wherein said second agent is distinct from said virus of said first agent and comprises nucleotides, wherein said first and second agents are associated with multiple sclerosis and are both purifiable from a viral isolate selected from the group consisting of POL-2 (ECAC V92072202) and MS7PG (ECAC V93010816).

2. A composition comprising: a first agent comprising an isolated virus, wherein said virus possesses reverse transcriptase activity, and a second agent, wherein said second agent is distinct from said virus of said first agent and comprises nucleotides, wherein said first and second agents are associated with multiple sclerosis and are both purifiable from a cell line selected from the group consisting of PLI-2 (ECAC 92072201) and LM7PC (ECAC 93010817).

3. A composition comprising: a first agent comprising an isolated virus which possesses reverse transcriptase activity, wherein said virus comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO;3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and sequences complementary to each of said SEQ ID NO:1 through SEQ ID NO:9; and a second agent distinct from said first agent, wherein said second agent comprises at least one antigen and a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10 through, SEQ ID NO:12.

4. The composition according to claim 1, wherein said first agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and sequences complementary to each of said SEQ ID NO:1 through SEQ ID NO:9.

5. The composition according to claim 1, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ NO:12.

6. The composition according to claim 4, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:12.

7. The composition according to claim 2, wherein said first agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and sequences complementary to each of said SEQ ID NO:1 through SEQ ID NO:9.

8. The composition according to claim 2, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ NO:12.

9. The composition according to claim 7, wherein said second agent comprises a nucleotide sequence selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, and sequences complementary to each of said SEQ ID NO:10, SEQ ID NO:11 and SEQ ID NO:12.

L1 ANSWER 11 OF 16 USPATFULL

1999:21732 Multiple sclerosis related virus.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy l'Etoile, France (non-U.S. corporation)
US 5871745 19990216
APPLICATION: US 1995-471969 19950606 (8)
PRIORITY: FR 1994-1529 19940204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:
1. An isolated virus comprising a nucleotide sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, and complementary sequences complementary thereto.

2. The isolated virus according to claim 1, wherein the nucleotide sequence is SEQ ID NO: 1 or a sequence complementary thereto.

3. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 2 or a sequence complementary thereto.

4. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 3 or a sequence complementary thereto.

5. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 4 or a sequence complementary thereto.

6. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 5 or a sequence complementary thereto.

7. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 6 or a sequence complementary thereto.

8. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 7 or a sequence complementary thereto.

9. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 8 or a sequence complementary thereto.

10. The isolated virus according to claim 1, wherein the nucleotide sequences is SEQ ID NO: 9 or a sequence complementary thereto.

L1 ANSWER 12 OF 16 USPATFULL
1998:104553 Detection of MSRV1 virus and MSRV2 pathogen and/or infective agent associated with multiple sclerosis, by nucleic acid hybridization.
Perron, Herve, Grenoble, France
Mallet, Francois, Villeurbanne, France
Mandrand, Bernard, Villeurbanne, France
Bedin, Frederic, Lyons, France
Beseme, Frederic, Villefontaine, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)
US 5800980 19980901
APPLICATION: US 1995-471724 19950606 (8)
PRIORITY: FR 1999-9401529 18990204
FR 1994-1530 19940204
FR 1994-1531 19940204
FR 1994-1532 19940204
FR 1994-14322 19941124
FR 1994-15810 19941223
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Composition including two pathogenic and/or infective agents associated with multiple sclerosis, namely a first agent which consists of a human virus possessing reverse transcriptase activity and related to a family of endogenous retroviral elements, or a variant of the virus, and a second agent, or a variant of the second agent, these two pathogenic and/or infective agents originating from the same viral strain chosen from the strains designated, respectively, POL-2 deposited with the ECACC on Jul. 22, 1992 under Accession Number V92072202 and MS7PG deposited with the ECACC on Jan. 8, 1993 under Accession Number V93010816, and from their variant strains.
CLM What is claimed is:

1. A method for distinguishing, in a biological sample, a viral material, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid of said viral material, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:20 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9; and distinguishing in said biological sample any said viral material having a sequence hybridized to said at least one probe.

2. The method according to claim 1, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one specific primer comprising a second nucleotide sequence selected from the group consisting of (i) SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a second complementary

sequence fully complementary to one of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a second homologous sequence sufficiently homologous with at least one second segment of at least 6 contiguous monomers of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said second complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9.

3. A method for distinguishing, in a biological sample, at least one pathogenic or infectious agent, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid or a complement of a nucleic acid of said pathogenic or infectious agent, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-2 and not to other naturally occurring nucleic acid sequences; and distinguishing in said biological sample any said at least one pathogenic or infectious agent having a sequence hybridized to said at least one probe.

4. The method according to claim 3, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one specific primer comprising a second nucleotide sequence selected from the group consisting of (i) SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, (ii) a second complementary sequence fully complementary to one of said SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37, and (iii) a second homologous sequence sufficiently homologous with at least one second segment of at least 6 contiguous monomers of said SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, or said second complementary sequence, to hybridize to a nucleic acid sequence of MSRV-2 and not to other naturally occurring nucleic acid sequences.

5. The method according to claim 1, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said viral material.

6. The method according to claim 1, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

7. The method according to claim 1, wherein a plurality of said probes

are employed.

8. The method according to claim 3, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said pathogenic or infectious agent.

9. The method according to claim 3, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

10. The method according to claim 3, wherein a plurality of said probes are employed.

11. A method for distinguishing, in a biological sample, a viral material associated with multiple sclerosis, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid of said viral material, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9; and distinguishing in said biological sample any said viral material having a sequence hybridized to said at least one probe.

12. The method according to claim 11, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said viral material.

13. The method according to claim 11, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

14. The method according to claim 11, wherein a plurality of said probes are employed.

15. A method for distinguishing, in a biological sample, at least one pathogenic or infectious agent associated with multiple sclerosis, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe which hybridizes with a nucleic acid or a complement of a nucleic acid of said pathogenic or infectious agent, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID

NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, or SEQ ID NO:37, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:13, SEQ ID NO:14, SEQ ID NO:15, SEQ ID NO:27, SEQ ID NO:28, SEQ ID NO:29, SEQ ID NO:30, SEQ ID NO:34, SEQ ID NO:35, SEQ ID NO:36, SEQ ID NO:37, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-2 and not to other naturally occurring nucleic acid sequences; and distinguishing in said biological sample any said at least one pathogenic or infectious agent having a sequence hybridized to said at least one probe.

16. The method according to claim 15, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said pathogenic or infectious agent.

17. The method according to claim 15, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

18. The method according to claim 15, wherein a plurality of said probes are employed.

19. A method for distinguishing, in a biological sample, a viral material, said method comprising contacting at least one nucleic acid from said biological sample, or at least one complementary nucleic acid complementary to said at least one nucleic acid, with at least one probe of not more than 100 contiguous monomers which hybridizes with a nucleic acid of said viral material, said probe comprising a first nucleotide sequence selected from the group consisting of (i) SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:16, SEQ ID NO:17, SEQ ID NO:18, SEQ ID NO:19, SEQ ID NO:20, SEQ ID NO:21, SEQ ID NO:22, SEQ ID NO:23, SEQ ID NO:24, SEQ ID NO:25, SEQ ID NO:26, SEQ ID NO:31, SEQ ID NO:32, SEQ ID NO:33, (ii) a first complementary sequence fully complementary to one of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26 or SEQ ID NO:31 through SEQ ID NO:33, and (iii) a first homologous sequence sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:3 through SEQ ID NO:7, SEQ ID NO:16 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9; and distinguishing in said biological sample any said viral material having a sequence hybridized to said at least one probe.

20. The method according to claim 19, wherein said at least one probe is specific for said nucleic acid or complementary nucleic acid of said viral material.

21. The method according to claim 19, wherein prior to contacting said at least one nucleic acid or complementary nucleic acid with said at least one probe, said at least one nucleic acid or complementary nucleic acid is amplified with at least one primer.

22. The method according to claim 19, wherein a plurality of said probes are employed.

23. The method according to claim 1, wherein said first homologous sequence is sufficiently homologous with at least one first segment of at least 6 contiguous monomers of said SEQ ID NO:4, SEQ ID NO:5, SEQ ID

NO:16, SEQ ID NO:17, SEQ ID NO:20 through SEQ ID NO:26, SEQ ID NO:31 through SEQ ID NO:33, or said first complementary sequence, to hybridize to a nucleic acid sequence of MSRV-1 and not hybridize to a nucleic acid sequence of HSERV9.

L1 ANSWER 15 OF 16 USPATFULL
97:63920 Process and culture medium for the production of cells infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy l' Etoile, France (non-U.S. corporation)
US 5650318 19970722
WO 9320188 19931014
APPLICATION: US 1994-157061 19940202 (8)
WO 1993-FR336 19930402 19940202 PCT 371 date 19940202 PCT 102(e) date
PRIORITY: FR 1992-4322 19920403
FR 1992-13443 19921103
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Process for in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), according to which a body sample is taken from an individual suffering from MS, said sample is cultivated in a culture medium which promotes the growth of infected cells to obtain a culture of primary infected cells, and a sample of the culture of primary cells or of a subculture of the latter is cultivated in series, that is to say by successive passages, in said culture medium to obtain the culture or cell line infected by a virus associated with MS, which comprises a procedure in which the culture medium also contains a beta anti-interferon antibody or an antibody which is directed against an antigenically close molecule, the antibody playing an inhibiting role in viral expression and allowing long-lasting expression and propagation of the viral strain in the culture or cell line.
CLM What is claimed is:
1. A process for the in vitro production of a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), said viral strain having at least one of its replication and expression inhibited by beta-interferon, said process comprising: obtaining a body sample from an individual suffering from MS, cultivating said sample in a culture medium which promotes the growth of infected cells to obtain a culture or cell line of primary infected cells, and cultivating by successive passages a sample of the culture or cell line of primary infected cells or a subculture of said culture or cell line in said culture medium to obtain the culture or cell line infected by a viral strain associated with MS, wherein the culture medium also contains an antibody that recognizes an epitope of beta-interferon, and said culture medium allows persistent expression and propagation of the viral strain in the culture or cell line.

2. The process as claimed in claim 1, wherein the body sample contains infected plexus choroideus cells.

3. A process for the production of a continuous infected culture or cell line comprising cells infected by at least one human viral strain associated with multiple sclerosis (MS) and whose replication is inhibited by beta-interferon, said process comprising the following steps: (a) cultivating human cells infected by said viral strain to obtain at least one primary culture infected by said viral strain, (b) cultivating non-infected human cells permissive to said viral strain to obtain at least one permissive culture, (c) cocultivating at least one

sample of the primary infected culture and at least one sample of the permissive culture to obtain a first derived culture infected by said viral strain, (d) cultivating the first derived infected culture in series by steps comprising cocultivation of a new sample of a permissive non-infected culture and a sample of the first derived infected culture or of a subculture of the first derived infected culture to obtain a new subculture of the same first derived infected culture constituting a continuous viral culture in non-immortal cells, at least any one of the culture steps (a) to (d) being carried out with a culture medium comprising an antibody that recognizes an epitope of beta-interferon.

4. The process as claimed in claim 3, wherein said human cells infected by said viral strain comprise at least one member selected from the group consisting of leptomeningeal cells, plexus choroideus cells, myeloid blood cells, and lymphocytes.

5. The process as claimed in claim 3, wherein said noninfected human cells comprise human plexus choroideus cells.

6. The process as claimed in claim 3, wherein said step (a) is carried out a plurality of times to provide a plurality of said primary cultures infected by differing viral strains, and step (c) is carried out by coculture of a sample of the permissive culture and of samples of said plurality of infected primary cultures.

7. A culture medium for carrying out a process as claimed in claim 1, comprising at least one amino acid, at least one vitamin factor, at least one inorganic salt and glucose, which comprises an anti-beta-interferon antibody.

8. A culture medium as claimed in claim 7, which comprises, in addition to the anti-beta-interferon antibody: between 400 and 2250 mg/l of said at least one amino acid, between 3.5 and 130 mg/l of said at least one vitamin factor, between 9100 and 13,000 mg/l of said at least one inorganic salt, and between 1000 and 6000 mg/l of glucose.

9. A biological cell material, which comprises cells sampled from or belonging to a culture or cell line infected by a viral strain associated with multiple sclerosis (MS), obtained by a process as claimed in claim 1, or derived cells obtained by modification of the genome of said cells without alteration of their phenotype.

10. The process as claimed in claim 3, wherein said human cells infected by said viral strain are selected from the group consisting of macrophages and monocytes.

11. A culture medium as claimed in claim 8, further comprising at least one growth factor selected from the group consisting of Endothelial Cell Growth Factor and basic Fibroblast Growth Factor.

12. A process for the production of a viable infected culture or cell line comprising cells infected by multiple sclerosis (MS), said process comprising: (a) cultivating MS infected human cells to obtain at least one culture or cell line of primary infected cells, (b) cultivating non-infected human cells that are permissive to MS to obtain at least one permissive culture, (c) cocultivating at least one sample of the primary infected culture or cell line of primary infected cells and at least one sample of the permissive culture to obtain a first derived infected culture, (d) cultivating the first infected derived culture in series, by cocultivating a new sample of a non-infected permissive culture and a sample of the first infected derived culture or of a

subculture of the first infected derived culture to obtain a new subculture of the same first infected derived culture, constituting a viable cell culture or cell line, wherein at least a portion of said process is carried out with a culture medium comprising an antibody that recognizes an epitope of beta-interferon.

13. The process according to claim 12, wherein said infected and non-infected human cells are nervous system cells.

14. The biological cell material as claimed in claim 9, wherein said cell line is cell line PLI-2, deposited at the ECACC on Jul. 22, 1992, under No. 92072201.

L1 ANSWER 16 OF 16 USPATFULL
96:116271 Process for the production of a viable cell culture infected by a multiple sclerosis-associated virus.
Perron, Herve, Grenoble, France
Seigneurin, Jean-Marie, Bernin, France
Bio Merieux, Marcy L'Etoile, France (non-U.S. corporation)Universite Joseph Fourier, Grenoble, France (non-U.S. corporation)
US 5585262 19961217
WO 9320189 19931014
APPLICATION: US 1994-157060 19940202 (8)
WO 1993-FR337 19930402 19940202 PCT 371 date 19940202 PCT 102(e) date
PRIORITY: FR 1992-4322 19920403
FR 1992-13447 19921103
DOCUMENT TYPE: Utility; Granted.
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to a process for in vitro culture of cells infected by a virus associated with multiple sclerosis and to the infected cell lines thus produced. The process is the cultivation of human cells infected by a viral strain to obtain at least one culture of primary cells infected by the said viral strain, along with the cultivation of non-infected human cells permissive to the viral strain to obtain at least one permissive culture, followed by cocultivation of at least one sample of a culture of infected primary cells and one sample of the permissive culture to obtain a first infected derived culture, then cultivating in series of the first infected derived culture. The invention is used in particular in the pharmaceutical diagnostics industry sector. In the preferred process, the infected cells are leptomeningeal cells and the permissive cells are leptomeningeal cells or plexuschoroideus cells.
CLM What is claimed is:
1. A process for producing a viable cell culture infected by at least one human viral strain associated with multiple sclerosis, said process comprising: (a) cultivating infected leptomeningeal cells to establish a primary culture of cells infected with said viral strain, (b) cultivating non-infected leptomeningeal cells or plexus choroideus cells to establish a permissive, non-infected culture, (c) cocultivating said infected cells from the primary culture with cells from the permissive culture to obtain a first derived culture of infected leptomeningeal cells or infected plexus choroideus cells; and (d) cocultivating cells from the derived culture with cells from the permissive culture to obtain a subculture of viable infected cells.

L2 ANSWER 1 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 2001-159475 [16] WPIDS
DNC C2001-047400
TI Detecting, preventing and treating degenerative, neurological and autoimmune diseases, particularly multiple sclerosis, using specified

polypeptides or related nucleic acid or ligand.
DC B04 D16
IN CHARLES, M H; KOLBE, H; MALCUS, C; PERRON, H; ROECKLIN, D; SANTORO, L; CHARLES, M
PA (INMR) BIOMERIEUX STELHYS SNC; (INMR) BIOMERIEUX STELHYS
CYC 95
PI WO 2001005422 A2 20010125 (200116)* FR 208p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
FR 2797402 A1 20010216 (200116)
AU 2000065768 A 20010205 (200128)
EP 1203239 A2 20020508 (200238) FR
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
ADT WO 2001005422 A2 WO 2000-FR2057 20000717; FR 2797402 A1 FR 1999-9372 19990715; AU 2000065768 A AU 2000-65768 20000717; EP 1203239 A2 EP 2000-953247 20000717, WO 2000-FR2057 20000717
FDT AU 2000065768 A Based on WO 200105422; EP 1203239 A2 Based on WO 200105422
PRAI FR 1999-9372 19990715
AB WO 200105422 A UPAB: 20010323
NOVELTY - Use of at least one polypeptide (A), containing at least fragment of a protein (B) selected from 28 sequences described in the specification, or having at least 70%, preferably 98% homology, to (B) or a fragment of one of the stated proteins, for detecting, preventing or treating a degenerative, neurological and/or auto-immune disease.

DETAILED DESCRIPTION - The sequences belong to the perlecan, precursor of the retinol-binding plasma protein, precursor of the ganglioside GM2 activator, calgranulin B or saposin B protein families.

INDEPENDENT CLAIMS are also included for the following:

(a) use of nucleic acids (C) that encode (A), or of the ligands (L) of (A) for detecting, preventing or treating a degenerative, neurological and/or autoimmune disease as for (A);

(b) use of (A) for preparation of immunogenic peptides;

(c) method for detecting (A), associated with a disease, by contacting (A) with (L) to form a complex of a complex or vice versa;

(d) polypeptide (A1) with a 193 amino acid sequence described in the specification, or fragments of it, provided these include at least one mutation relative to another 193 amino acid sequence (8) described in the specification;

(e) use of (A1) in the same ways as (A);

(f) nucleic acid (C1) encoding (A1);

(g) use of (C1) in the same ways as (C);

(h) method for detecting (A) and (A1) by mass spectrometry;

(i) diagnostic and prognostic method based on measuring at least one (A);

(j) use of (A), (C) or recombinant proteins encoded by (C), for testing the efficacy of therapeutic agents or for producing a pharmaceutical composition; and

(k) use of lycorin to produce a composition for preventing or treating a degenerative, neurological and/or autoimmune disease.

ACTIVITY - Antineurodegeneration; Immunomodulatory.

MECHANISM OF ACTION - Vaccine; Gene therapy.

USE - (A), also nucleic acid (C) encoding them and ligands of (A) and (C), are especially used for diagnosis, prognosis, prevention and treatment of multiple sclerosis (in its various forms and phases), but may also be useful in cases of e.g. Alzheimer's and Parkinson's diseases, amyotrophic lateral sclerosis, rheumatoid polyarthritis and lupus

erythematosus, including use as vaccines and in gene therapy (expression of sense or antisense sequences). They can also be used to assess efficacy of potential therapeutic agents, particularly compounds that reduce or inhibit toxicity towards glial cells.
Dwg.0/18

L2 ANSWER 3 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 2000-506097 [45] WPIDS
DNN N2000-374240 DNC C2000-151974
TI Nucleotide fragment of LTR-RU5 region from Multiple Sclerosis retrovirus (MSRV) used to detect the presence of MSRV-1 retrovirus in a biological sample.
DC B04 D16 S03
IN BACCALA-PARANHOS, G; KOMURIAN-PRADEL, F; PERRON, H; PARANHOS-BACCALA, G
PA (INMR) BIO MERIEUX
CYC 91
PI WO 2000047745 A1 20000817 (200045)* EN 23p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
EP 1029917 A1 20000823 (200046) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
AU 2000024566 A 20000829 (200062)
EP 1151108 A1 20011107 (200168) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI
JP 2002536019 W 20021029 (200274) 27p
ADT WO 2000047745 A1 WO 2000-IB159 20000215; EP 1029917 A1 EP 1999-420041 19990215; AU 2000024566 A AU 2000-24566 20000215; EP 1151108 A1 EP 2000-902825 20000215, WO 2000-IB159 20000215; JP 2002536019 W JP 2000-598643 20000215, WO 2000-IB159 20000215
FDT AU 2000024566 A Based on WO 200047745; EP 1151108 A1 Based on WO 200047745; JP 2002536019 W Based on WO 200047745
PRAI EP 1999-420041 19990215
AB WO 200047745 A UPAB: 20000918
NOVELTY - Nucleotide fragment (I) of a long terminal repeat (LTR)-RU5 region comprising a nucleotide sequence which encodes the expression of an Multiple Sclerosis retrovirus (MSRV-1) protein (II) and a complementary nucleotide fragment, are new.

DETAILED DESCRIPTION - Nucleotide fragment of a LTR-RU5 region comprises a nucleotide sequence which encodes the expression of a protein (II). (II) comprises a peptide sequence from MSRV-1 retrovirus of (III), (IV) or (V) of 76, 64 and 140 amino acids (aa) respectively.

INDEPENDENT CLAIMS are also included for the following:

(1) a nucleic acid probe for the detection of MSRV-1 retrovirus which comprises 10-1000 monomers and specifically hybridizes with (I) in high stringency conditions;

(2) a primer for the amplification by polymerization of a nucleic acid retroviral sequence of MSRV-1 virus which comprises 10-30 monomers and hybridizes to (I) in high stringency conditions;

(3) a protein (II) encoded by (I);

(4) a polypeptide (VI) comprising at least 6 aa of (V);

(5) a polyclonal or monoclonal antibody directed against (II) or (VI);

(6) a process for detecting in a biological sample the presence of MSRV-1 retrovirus comprising contacting a probe of (1) with the biological

sample and determining whether the probe binds to nucleic acid in the sample, where binding indicates the presence of MSRV-1 retrovirus;

(7) a process for detecting in a biological sample the presence of MSRV-1 retrovirus comprising contacting an antibody of (5) with the biological sample and determining whether the antibody binds to protein in the sample, where binding indicates the presence of MSRV-1 retrovirus; and

(8) a process for detecting in a biological sample the presence of MSRV-1 retrovirus comprising detecting the antigenic or biological properties of (II) or a fragment of (II).

USE - The probes and antibodies to MSRV-1 retrovirus protein are used to detect the presence of MSRV-1 retrovirus in a biological sample (claimed). The detection process can be used to identify and quantify, separate or isolate the substance or agent.

Dwg.0/3

L2 ANSWER 6 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 1999-098275 [09] WPIDS
DNC C1999-029242
TI Nucleic acid sequences of retrovirus called MSRV-1 - associated with multiple sclerosis or rheumatoid polyarthritis.
DC B04 D16
IN BEDIN, F; KOMURIAN-PRADEL, F; MALLET, F; MANDRAND, B; OTT, C; PARAHNOS-BACCALA, G; PERRON, H; SODOYER, M
PA (INMR) BIO MERIEUX
CYC 84
PI FR 2765588 A1 19990108 (199909)* 82p
WO 9902666 A2 19990121 (199910) FR
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH GM GW HR HU ID IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9885450 A 19990208 (199924)
EP 996731 A2 20000503 (200026) FR
R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2002509437 W 20020326 (200236) 101p
ADT FR 2765588 A1 FR 1997-8816 19970707; WO 9902666 A2 WO 1998-FR1460 19980707; AU 9885450 A AU 1998-85450 19980707; EP 996731 A2 EP 1998-936467 19980707, WO 1998-FR1460 19980707; JP 2002509437 W WO 1998-FR1460 19980707, JP 1999-508255 19980707
FDT AU 9885450 A Based on WO 9902666; EP 996731 A2 Based on WO 9902666; JP 2002509437 W Based on WO 9902666
PRAI FR 1997-8816 19970707
AB FR 2765588 A UPAB: 19990302
The following are claimed:

(1) isolated or purified nucleic acid material comprising a nucleotide sequence selected from (i) the 310 bp, 635 bp, 1481 bp, 1329 bp, 1511 bp, 764 bp, 800 bp sequences given in the specification; (ii) sequences complementary to the sequences of (i); and (iii) sequences equivalent to the sequences of (i) and (ii), especially sequences having at least 50%, preferably at least 70%, homology with the sequences of (i) or (ii) for any stretch of 100 contiguous monomers; (2) isolated or purified nucleic acid material encoding a polypeptide having at least 50%, preferably at least 70%, homology with a peptide sequence selected from the 103, 77, 493, 162, 398 and 378 amino acid sequences given in the specification for any contiguous stretch of at least 30 amino acids; (3) retroviral nucleic acid material in which the pol gene comprises a nucleotide sequence identical or equivalent to the 310 bp sequence and its complements; (4) retroviral nucleic acid material in which the 5' end of the pol gene starts at nucleotide 1419 of the 1511bp sequence; (5)

retroviral nucleic acid material in which the pol gene encodes a polypeptide having at least 50%, preferably at least 70%, homology with the 103 amino acid sequence for any contiguous stretch of at least 30 amino acids; (6) retroviral nucleic acid material in which the 3' end of the gag gene ends at nucleotide 1418 of 1511bp sequence; (7) retroviral nucleic acid material in which the env gene comprises a nucleotide sequence identical or equivalent to a sequence selected from 1481bp sequence and its complement; (8) retroviral nucleic acid material in which the env gene comprises a nucleotide sequence that starts at nucleotide 1 of the 1481 bp sequence and ends at nucleotide 233 of the 635 bp sequence; (9) retroviral nucleic acid material in which the env gene encodes a polypeptide having at least 50%, preferably at least 70%, homology with the 493 aa sequence for any contiguous stretch of at least 30 amino acids; (10) retroviral nucleic acid material in which the U3R region of the 3' LTR comprises a nucleotide sequence that ends at nucleotide 617 of the 635 bp sequence; (11) retroviral nucleic acid material in which the RU5 region of the 5' LTR comprises a nucleotide sequence that starts at nucleotide 755 of 1329 bp sequence and ends at nucleotide 337 of the 764 bp sequence or the 800 bp sequence; (12) retroviral nucleic acid material comprising a sequence that starts of nucleotide 755 of the 1329bp sequence and ends at nucleotide 617 of the 635bp sequence; (13) retroviral nucleic acid material as in (1)-(12) that is associated with at least one autoimmune disease such as multiple sclerosis or rheumatoid polyarthritis; (14) a nucleotide fragment comprising a nucleotide sequence as in (1); (15) a nucleotide fragment comprising a nucleotide sequence encoding a polypeptide as in (2); (16) a nucleic acid probe for detecting a retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, capable of specifically hybridising to a fragment as in (14) or (15) belonging to the genome of the retrovirus; (17) a primer for amplifying RNA or DNA of a retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, comprising a nucleotide sequence identical or equivalent to at least a portion of the nucleotide sequence of a fragment as in one of (8)-(11), especially a sequence having at least 50%, preferably at least 70%, homology with this portion for any stretch of 10 contiguous monomers; (18) RNA or DNA, especially a replication and/or cloning vector, comprising a genomic fragment of nucleic acid material as in one of (1)-(7) or a fragment as in (14) or (15); (19) a peptide encoded by any open reading frame belonging to a nucleotide fragment as in (14) or (15), especially a polypeptide, e.g. an oligopeptide, forming or comprising an antigenic determinant recognised by the sera of patients infected with the virus MSRV-1 and/or in whom the MSRV-1 virus has been reactivated.

USE - Also claimed are: (20) a diagnostic, prophylactic or therapeutic composition for inhibiting expression of at least one retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, comprising a nucleotide fragment as in (14) or (15); (21) a method for detecting a retrovirus associated with multiple sclerosis and/or rheumatoid polyarthritis, comprising contacting RNA and/or DNA presumed to belong to or originate from the retrovirus, or the corresponding complementary RNA and/or DNA, with a composition comprising a nucleotide fragment as in (14) or (15).

Dwg.0/11

L2 ANSWER 10 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 1998-322732 [28] WPIDS
DNN N1998-252312 DNC C1998-099357
TI New nucleic acid from retroviruses - useful for diagnosis, prevention and treatment of, e.g. multiple sclerosis.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; JOLIVET-REYNAUD, C; KOMURIAN-PRADEL, F; MANDRAND, B; PARANHOS-BACCALA, G; PERRON, H

PA (INMR) BIO MERIEUX
CYC 20
PI WO 9823755 A1 19980604 (199828)* EN 286p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP
EP 942987 A1 19990922 (199943) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
JP 2001505768 W 20010508 (200131) 279p
ADT WO 9823755 A1 WO 1997-IB1482 19971126; EP 942987 A1 EP 1997-911411 19971126, WO 1997-IB1482 19971126; JP 2001505768 W WO 1997-IB1482 19971126, JP 1998-524475 19971126
FDT EP 942987 A1 Based on WO 9823755; JP 2001505768 W Based on WO 9823755
PRAI US 1996-756429 19961126
AB WO 9823755 A UPAB: 19980715
Isolated or purified nucleic acid (I) is: (a) a sequence of 2304 (S1) or 2364 (S2) bp respectively; (b) equivalents of S1 and S2, particularly sequences having for any 100 contiguous nt at least 50 (especially 80)% homology with (a), or (c) their complements, excluding HSERV-9 (human sequence of endogenous retrovirus-9) sequences. Also new are: (1) nucleic acid (Ia) encoding any polypeptide (II) having, for at least 30 contiguous aa, at least 50 (especially 70) % homology with a peptide encoded by S1, S2 or their complements; (2) nucleic acid (Ia) of retroviral type identical, or equivalent, to at least 1 part of the pol gene of isolated retrovirus associated with multiple sclerosis (MS) or rheumatoid arthritis (RA); (3) probes (II) that hybridise to (I); (4) primers derived from (I); (5) polypeptides (III) encoded by (I); (6) polypeptides (IV) that inhibit activity of (III), and (7) mono- or poly-clonal antibody (Ab) against MS associated retrovirus-1 (MSRV-1) raised against antigenic (III).
USE - (II), (III) and Ab are used to detect MSRV-1, or exposure to it, by usual immunoassay/hybridisation techniques.(I), (II) and Ab are used to diagnose infection by MS and RA-associated viruses, and also for prevention and treatment of infection with these viruses.
Dwg.0/53

L2 ANSWER 13 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 1997-154266 [14] WPIDS
DNN N1997-127420 DNC C1997-049375
TI New viral material and nucleotide fragments associated with multiple sclerosis and rheumatoid arthritis - also related peptide(s) and antibodies, used for diagnosis, treatment and as vaccines.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; JOLIVET-REYNAUD, C; KOMURIAN-PRADEL, F; MANDRAND, B; PARANHOS-BACCALA, G; PERRON, H; JOLIVET, R C; KOMURIAN, P F; PARANHOS, B G; PARANHOSBACCALA, G
PA (INMR) BIO MERIEUX
CYC 72
PI WO 9706260 A1 19970220 (199714)* FR 188p
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN
FR 2737500 A1 19970207 (199715) 107p
AU 9668232 A 19970305 (199726)
NO 9701493 A 19970603 (199733)
EP 789077 A1 19970813 (199737) FR 121p
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
BR 9606566 A 19971230 (199807)
CZ 9701357 A3 19980617 (199830)
SK 9700567 A3 19980909 (199848)
JP 11502416 W 19990302 (199919) 178p

NZ 316080 A 19990429 (199923)
HU 9900425 A2 19990528 (199930)
US 6001987 A 19991214 (200005)
AU 730080 B 20010222 (200115)

ADT WO 9706260 A1 WO 1996-FR1244 19960802; FR 2737500 A1 FR 1995-9643 19950803; AU 9668232 A AU 1996-68232 19960802; NO 9701493 A WO 1996-FR1244 19960802, NO 1997-1493 19970402; EP 789077 A1 EP 1996-420265 19960802; BR 9606566 A BR 1996-6566 19960802, WO 1996-FR1244 19960802; CZ 9701357 A3 WO 1996-FR1244 19960802, CZ 1997-1357 19960802; SK 9700567 A3 WO 1996-FR1244 19960802, SK 1997-567 19960802; JP 11502416 W WO 1996-FR1244 19960802, JP 1997-508179 19960802; NZ 316080 A NZ 1996-316080 19960802, WO 1996-FR1244 19960802; HU 9900425 A2 WO 1996-FR1244 19960802, HU 1999-425 19960802; US 6001987 A US 1996-691563 19960802; AU 730080 B AU 1996-68232 19960802

FDT AU 9668232 A Based on WO 9706260; BR 9606566 A Based on WO 9706260; CZ 9701357 A3 Based on WO 9706260; JP 11502416 W Based on WO 9706260; NZ 316080 A Based on WO 9706260; HU 9900425 A2 Based on WO 9706260; AU 730080 B Previous Publ. AU 9668232, Based on WO 9706260

PRAI FR 1995-9643 19950803

AB WO 9706260 A UPAB: 19970407
Isolated and purified viral material (A) includes, in the genome, (a) one of 10 sequences given in the specification (from about 400 bp to 2.5 kb); (b) their complements or (c) sequences equiv. to (a) and (b) and having at least 50, pref. 70, % homology with (a) and (b) over a stretch of 100 contiguous nucleotides. New nucleotide fragments (B) comprise: (i) any complete or partial genomic sequence of the pol gene of virus MSRV-1 (multiple sclerosis related virus), excluding a specified 1158 bp sequence (S1); (ii) all partial or complete genomic env or gag gene sequence of MSRV-1; (iii) any sequence that overlaps the pol and env or pol and gag genes; (iv) any partial or complete sequence from those 10 sequences from (A) given in the specification, i.e. from the clones FBd3, t pol, JLBc1, JLBc2, GM3, FBd13, LB19, LTRGAG12, FP6 and G+E+A, but excluding sequences identical to, or contg., S1; (v) sequences complementary to the above genomic sequences; (vi) any equiv. sequence; (B) does not comprise or include the ERV (endogenous retroviral)-9 sequence.

USE - All 10 of the sequences (A) are associated with MS; 6 are also associated with RA. (C) and Ab are useful for detection of MSRV-1 (or its specific antibodies), also for prevention and treatment, e.g. as a vaccine. (B) and related nucleic acid can be used similarly to detect infectious agents by hybridisation and to inhibit expression of these pathogens.

ADVANTAGE - MS and RA can now be detected at an early stage before symptoms are manifest.

Dwg.0/42

L2 ANSWER 16 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 1995-283776 [37] WPIDS
DNN N1995-215943 DNC C1995-128080
TI Two pathogenic or infectious agents associated with multiple sclerosis - one being a retrovirus, useful for early diagnosis, prevention and treatment.
DC B04 D16 S03
IN BEDIN, F; BESEME, F; MALLET, F; MANDRAND, B; PERRON, H
PA (INMR) BIO MERIEUX
CYC 59
PI WO 9521256 A1 19950810 (199537)* FR 104p
RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ
W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP KR KZ LK LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN
FR 2715936 A1 19950811 (199537) 33p
FR 2715937 A1 19950811 (199537) 69p

FR 2715938 A1 19950811 (199537) 32p
FR 2715939 A1 19950811 (199537) 39p
CA 2141907 A 19950805 (199543) FR
EP 674004 A1 19950927 (199543) FR 60p
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
AU 9517114 A 19950821 (199547)
FI 9504699 A 19951003 (199601)
NO 9503925 A 19951204 (199606)
FR 2727428 A1 19960531 (199629) 55p
FR 2728585 A1 19960628 (199633) 65p
JP 08511170 W 19961126 (199708) 100p
NZ 279855 A 19980527 (199827)
US 5800980 A 19980901 (199842)
US 5871745 A 19990216 (199914)
US 5871996 A 19990216 (199914)
AU 704440 B 19990422 (199927)
US 5962217 A 19991005 (199948)
US 6184025 B1 20010206 (200109)
US 6342383 B1 20020129 (200210)

ADT WO 9521256 A1 WO 1995-FR142 19950206; FR 2715936 A1 FR 1994-1529 19940204; FR 2715937 A1 FR 1994-1532 19940204; FR 2715938 A1 FR 1994-1530 19940204; FR 2715939 A1 FR 1994-1531 19940204; CA 2141907 A CA 1995-2141907 19950206; EP 674004 A1 EP 1995-420027 19950206; AU 9517114 A AU 1995-17114 19950206; FI 9504699 A WO 1995-FR142 19950206, FI 1995-4699 19951003; NO 9503925 A WO 1995-FR142 19950206, NO 1995-3925 19951003; FR 2727428 A1 FR 1994-14322 19941124; FR 2728585 A1 FR 1994-15810 19941223; JP 08511170 W JP 1995-520426 19950206, WO 1995-FR142 19950206; NZ 279855 A NZ 1995-279855 19950206, WO 1995-FR142 19950206; US 5800980 A Div ex US 1995-384137 19950206, US 1995-471724 19950606; US 5871745 A Div ex US 1995-384137 19950206, US 1995-471969 19950606; US 5871996 A US 1995-384137 19950206; AU 704440 B AU 1995-17114 19950206; US 5962217 A Div ex US 1995-384137 19950206, US 1995-470006 19950606; US 6184025 B1 Div ex US 1995-384137 19950206, Div ex US 1995-471969 19950606, US 1998-200990 19981130; US 6342383 B1 Div ex US 1995-384137 19950206, US 1998-133411 19980813

FDT AU 9517114 A Based on WO 9521256; JP 08511170 W Based on WO 9521256; NZ 279855 A Based on WO 9521256; AU 704440 B Previous Publ. AU 9517114, Based on WO 9521256; US 5962217 A Div ex US 5871996; US 6184025 B1 Div ex US 5871745, Div ex US 5871996; US 6342383 B1 Div ex US 5871996

PRAI FR 1994-15810 19941223; FR 1994-1529 19940204; FR 1994-1530 19940204; FR 1994-1531 19940204; FR 1994-1532 19940204; FR 1994-14322 19941124

AB WO 9521256 A UPAB: 19950921
Compsn. (A) comprises 2 pathogenic and/or infectious agents, isolated or purified, associated with multiple sclerosis i.e. (1) agent (Ia) that is a human virus with reverse transcriptase activity and of the endogenous retroviral family, or its variant and (2) agent (Ib) or its variant. (Ia) and (Ib) are derived from the same viral strain, i.e. POL-2 (ECACC V92072202) or MS7PG (ECACC V93010816), or their variants. Alternatively (Ia) and (Ib) are produced by the same cell line, i.e. PLI-2 (ECACC 92072201) or LM7PC (ECACC 93010817) or other similar infected cell cultures.

USE - Nucleic acid fragments contg. sequences (1)-(12) are used for detecting agents associated with multiple sclerosis, also for prophylaxis and treatment. Probes of (6) may be used to separate and identify these agents, opt. in conjunction with amplification primers. (III), and antibodies specific for them, can also be used for diagnosis, prophylaxis and therapy.

ADVANTAGE - Detection of the infectious agent allows early diagnosis of disease, before neurological symptoms appear.
Dwg.0/17

L2 ANSWER 18 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 1993-336897 [42] WPIDS
CR 1993-336896 [42]
DNC C1993-149082
TI Viable cell culture infected with multiple sclerosis virus - prepd. by co-culturing prim. infected and permissive cells, then passaging, for virus identification and characterisation.
DC B04 D16
IN PERRON, H; SEIGNEURIN, J
PA (INMR) BIO MERIEUX; (UYGR-N) UNIV GRENOBLE FOURIER JOSEPH; (UYFO-N) UNIV FOURIER JOSEPH; (UYFO-N) UNIV FOURIER FOURIER
CYC 19
PI WO 9320189 A1 19931014 (199342)* FR 24p
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA US
EP 592636 A1 19940420 (199416) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5585262 A 19961217 (199705) 6p
EP 592636 B1 19981125 (199851) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69322227 E 19990107 (199907)
US 5925555 A 19990720 (199935)
ADT WO 9320189 A1 WO 1993-FR337 19930402; EP 592636 A1 EP 1993-908990 19930402, WO 1993-FR337 19930402; US 5585262 A WO 1993-FR337 19930402, US 1994-157060 19940202; EP 592636 B1 EP 1993-908990 19930402, WO 1993-FR337 19930402; DE 69322227 E DE 1993-622227 19930402, EP 1993-908990 19930402, WO 1993-FR337 19930402; US 5925555 A Div ex WO 1993-FR337 19930402, Div ex US 1994-157060 19940202, US 1996-651573 19960522
FDT EP 592636 A1 Based on WO 9320189; US 5585262 A Based on WO 9320189; EP 592636 B1 Based on WO 9320189; DE 69322227 E Based on EP 592636, Based on WO 9320189; US 5925555 A Div ex US 5585262
PRAI FR 1992-4322 19920403; FR 1992-13447 19921103
AB WO 9320189 A UPAB: 19931202
A viable, infected culture or cell line, comprising cells infected with at least one strain of the human virus associated with multiple sclerosis, is made by (1) growing human cells infected with the virus and, separately, non-infected permissive cells; (2) co-culturing samples of infected and permissive cells to give a first derived culture infected with virus; (3) cultivating the culture in series. Step (3) involves repeating the co-culture step using a new sample of permissive culture plus a sample of first derived culture (or its subculture) to give a new subculture which constitutes the viable viral culture.

Also new are (1) the infected cells (withdrawn from or belonging to the cultures prepd. as described), and derived cells in which the genome has been altered without changing the phenotype, and (2) a culture medium for use in the process.

Primary infected cells are pref. leptomeningeal cells; choroid plexus cells; nyeloid blood cells (esp. macrophages or monocytes) or lymphocytes, and permissive cells are esp. choroid plexus cells.

USE/ADVANTAGE - These cultures are partic. useful for identification and characterisation of the virus, but could also have clinical or therapeutic application. They provide good replication and viral expression.
Dwg.0/2

L2 ANSWER 19 OF 19 WPIDS (C) 2002 THOMSON DERWENT
AN 1993-336896 [42] WPIDS
CR 1993-336897 [42]
DNN N1993-260345 DNC C1993-149081
TI Prodn. of cultures and cell lines contg. multiple sclerosis virus - by

growing infected cells in medium contg. antibody against beta-interferon, also derived cells and viral material, useful e.g. in vaccines and diagnosis.

DC B04 D16 S03

IN PERRON, H; SEIGNEURIN, J; PERRON, A; RRON, H

PA (INMR) BIO MERIEUX; (UYGR-N) UNIV GRENOBLE FOURIER JOSEPH; (UYFO-N) UNIV FOURIER JOSEPH

CYC 19

PI WO 9320188 A1 19931014 (199342)* FR
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL PT SE
W: CA US
FR 2689519 A1 19931008 (199348) 16p
FR 2689520 A1 19931008 (199348) 38p
FR 2689521 A1 19931008 (199348) 20p
EP 587873 A1 19940323 (199412) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 592636 A1 19940420 (199416) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
US 5585262 A 19961217 (199705) 6p
US 5650318 A 19970722 (199735) 14p
EP 957162 A1 19991117 (199953) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
EP 587873 B1 20000119 (200009) FR
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
DE 69327623 E 20000224 (200017)
ES 2142864 T3 20000501 (200028)
US 6071736 A 20000606 (200033)
US 6291225 B1 20010918 (200157)
CA 2110703 C 20011204 (200203) FR

ADT WO 9320188 A1 WO 1993-FR336 19930402; FR 2689519 A1 FR 1992-4322 19920403; FR 2689520 A1 FR 1992-13443 19921103; FR 2689521 A1 FR 1992-13447 19921103; EP 587873 A1 EP 1993-908989 19930402, WO 1993-FR336 19930402; EP 592636 A1 EP 1993-908990 19930402, WO 1993-FR337 19930402; US 5585262 A WO 1993-FR337 19930402, US 1994-157060 19940202; US 5650318 A WO 1993-FR336 19930402, US 1994-157061 19940202; EP 957162 A1 Div ex EP 1993-908989 19930402, EP 1999-113896 19930402; EP 587873 B1 EP 1993-908989 19930402, WO 1993-FR336 19930402, Related to EP 1999-113896 19930402; DE 69327623 E DE 1993-627623 19930402, EP 1993-908989 19930402, WO 1993-FR336 19930402; ES 2142864 T3 EP 1993-908989 19930402; US 6071736 A Cont of US 1994-157061 19940202, US 1996-754010 19961120; US 6291225 B1 Div ex WO 1993-FR336 19930402, Div ex US 1994-157061 19940202, US 1995-485145 19950607; CA 2110703 C CA 1993-2110703 19930402, WO 1993-FR336 19930402

FDT EP 587873 A1 Based on WO 9320188; EP 592636 A1 Based on WO 9320189; US 5585262 A Based on WO 9320189; US 5650318 A Based on WO 9320188; EP 957162 A1 Div ex EP 587873; EP 587873 B1 Related to EP 957162, Based on WO 9320188; DE 69327623 E Based on EP 587873, Based on WO 9320188; ES 2142864 T3 Based on EP 587873; US 6071736 A Cont of US 5650318; US 6291225 B1 Div ex US 5650318; CA 2110703 C Based on WO 9320188

PRAI FR 1992-13443 19921103; FR 1992-4322 19920403

AB WO 9320188 A UPAB: 20020114
A culture or cell line infected with a virus strain associated with multiple sclerosis (MS) is prepd. by (1) taking a body sample from an MS patient; (2) culturing this in medium favouring growth of infected cells to produce a culture of primary infected cells; (3) subjecting a sample of this (or of derived subculture) to successive passaging. The culture medium used contains an antibody (Ab) against beta-interferon (or an antigenically similar cpd.) which acts as an inhibitor of viral expression, to allow persistent expression of virus and propagation of the viral strain in the culture or cell line.

Also new are (1) prodn. of continuous cultures or cell lines infected with the viral; (2) culture media contg. Ab; (3) cell withdrawn from (or

belonging to) cultures produced as above (also their derivs. in which the genome has been modified without affecting the phenotype); (4) method for transactivation of MS-related virus in such cells; (5) virus fractions isolated from these cells; and (6) immunological reactant comprising mono- or poly-clonal antibodies directed against antigenic viral extracts.

USE/ADVANTAGE - Antigenic extracts of the infected cells, or the new viral material (killed, inactivated or attenuated) are useful in vaccines and for detecting antibodies specific for MS-related virus.

L3 ANSWER 4 OF 37 MEDLINE
2001072824 Document Number: 20070778. PubMed ID: 10602665. Human retroviral sequences associated with extracellular particles in autoimmune diseases: epiphenomenon or possible role in aetiopathogenesis?. Perron H; Seigneurin J M. (BioMerieux SA, Chemin de l'Orme 69280 Marcy l'Etoile, France.) Microbes Infect, (1999 Apr) 1 (4) 309-22. Ref: 64. Journal code: 100883508. ISSN: 1286-4579. Pub. country: France. Language: English.
AB Publications describing retroviral sequences associated with extracellular particles in Sjogren's syndrome or systemic lupus erythematosus, multiple sclerosis, and type I diabetes present novel arguments and raise complex questions about eventual relationships between retroviruses and autoimmunity. They are presented and discussed in the present review, preceded by an overview of the biology of retroviral elements.

L3 ANSWER 5 OF 37 MEDLINE
2001030746 Document Number: 20444379. PubMed ID: 10986298. Infrequency of detection of particle-associated MSRV/HERV-W RNA in the synovial fluid of patients with rheumatoid arthritis. Gaudin P; Ijaz S; Tuke P W; Marcel F; Paraz A; Seigneurin J M; Mandrand B; Perron H; Garson J A. (Department of Virology, Royal Free and University College Medical School, London, UK.) RHEUMATOLOGY, (2000 Sep) 39 (9) 950-4. Journal code: 100883501. ISSN: 1462-0324. Pub. country: ENGLAND: United Kingdom. Language: English.
AB OBJECTIVES: To determine whether the recently identified multiple sclerosis-associated retrovirus, MSRV, is detectable in the serum and synovial fluid of patients with rheumatoid arthritis (RA). METHODS: A reverse transcription-polymerase chain reaction (RT-PCR) assay was used to seek evidence of particle-associated MSRV/HERV-W RNA in the plasma and synovial fluid of patients with RA and controls. Stringent precautions were taken to avoid detection of contaminating human genomic DNA and cellular RNA sequences. RESULTS: Thirty-seven plasma samples were tested (20 from RA patients and 17 from controls) but none had detectable MSRV/HERV-W RNA. Synovial fluid samples were available from nine patients with RA and 10 controls. Particle-associated MSRV/HERV-W RNA was reproducibly detected in two of nine synovial fluid samples from RA patients and in one control sample. The identity of RT-PCR products was confirmed by sequencing. CONCLUSION: MSRV/HERV-W RNA sequences are detectable in the synovial fluid of a small proportion of RA patients, but this phenomenon may not be specific to RA.

L3 ANSWER 6 OF 37 MEDLINE
2000332466 Document Number: 20332466. PubMed ID: 10871789. Particle-associated retroviral RNA and tandem RGH/HERV-W copies on human chromosome 7q: possible components of a 'chain-reaction' triggered by infectious agents in multiple sclerosis?. Perron H; Perin J P; Rieger F; Alliel P M. (BioMerieux STELHYS, Chemin de l'Orme, 69280 Marcy l'Etoile, France.) JOURNAL OF NEUROVIROLOGY, (2000 May) 6 Suppl 2 S67-75. Ref: 33. Journal code: 9508123. ISSN: 1355-0284. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Different groups have observed retrovirus particle (RVP) production in cell cultures from patients with multiple sclerosis (MS). This in vitro production appeared relatively specific for MS versus healthy controls, but was likely to be enhanced or activated by infectious triggers such as Herpesviruses (e.g. HSV, EBV). Independent molecular analysis of retroviral RNA associated with RVP revealed two different genetic families of endogenous retroviral elements (HERV): MSRV/HERV-W and RGH/HERV-H. Interestingly, these sequences were detected by mutually exclusive primers in RT - PCR amplifications. Surprisingly, these two HERV families both contain an ancestral proviral copy inserted in chromosome 7q21-22 region

at about 1 kb of distance of each other. Another HERV-W proviral sequence is located within a T-cell alpha-delta receptor (TCR) gene in chromosome 14q11.2 region. Interestingly, these two regions correspond to genetic loci previously identified as potentially associated with 'multigenic' susceptibility to MS and TCR alpha chain genetic determinants have been reported to be statistically associated with MS. A plausible role for infectious agents triggering a co-activation of the chromosome 7q HERV tandem (replicative retrovirus and/or other virus and/or intracellular bacteria) and, eventually, other HERV copies, is discussed. The role of particular HERV polymorphism and the production of pathogenic molecules (gliotoxin and superantigen) possibly associated with retroviral expression are also evoked. An integrative concept of pathogenic 'chain-reaction' in MS involving several step-specific pathogenic 'agents' and 'products' somewhat interacting with particular genetic elements would federate most partial data obtained on MS, including retroviral expression.

L3 ANSWER 8 OF 37 MEDLINE
2000046348 Document Number: 20046348. PubMed ID: 10580403. Phylogeny of a novel family of human endogenous retrovirus sequences, HERV-W, in humans and other primates. Voisset C; Blancher A; Perron H; Mandrand B; Mallet F; Paranhos-Baccala G. (Unite Mixte de Recherche 103 CNRS-bioMerieux, Ecole Normale Superieure de Lyon, France.) AIDS RESEARCH AND HUMAN RETROVIRUSES, (1999 Nov 20) 15 (17) 1529-33. Journal code: 8709376. ISSN: 0889-2229. Pub. country: United States. Language: English.
AB A novel human endogenous retrovirus, HERV-W, has been characterized on the basis of multiple sclerosis-associated retrovirus (MSRV) probes. We have analyzed the phylogenetic distribution of HERV-W in humans and other primate species. As HERV-W presents a C/D chimeric nature and is largely composed of deleted elements, Southern blots were performed using gag, pol, env, and LTR probes. The relative complexities observed for gag, pol, env, and LTR regions were similar in humans, apes, and Old World monkeys, the minimal number of bands observed after Southern blot analysis being 25, 50, 10, and at least 100, respectively. The HERV-W family entered the genome of catarrhines more than 25 million years ago.

L3 ANSWER 9 OF 37 MEDLINE
1999335590 Document Number: 99335590. PubMed ID: 10405350. Molecular cloning and characterization of MSRV-related sequences associated with retrovirus-like particles. Komurian-Pradel F; Paranhos-Baccala G; Bedin F; Ounanian-Paraz A; Sodoyer M; Ott C; Rajoharison A; Garcia E; Mallet F; Mandrand B; Perron H. (Ecole Normale Superieure de Lyon, UMR 103 CNRS-bioMerieux, 46, Allee d'Italie, Lyon Cedex 07, 69364, France.) VIROLOGY, (1999 Jul 20) 260 (1) 1-9. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.
AB New sequences have been obtained by successive overlapping RT-PCR extensions from the pol region of a retroviral RNA (multiple sclerosis-associated retroviral element, MSRV) amplified in retrovirus-like particles from patients with multiple sclerosis. gag and pol sequences are related to type C oncoviruses, whereas the env sequence is closer to type D. A tryptophan-like (W) tRNA primer-binding site was identified downstream of the RU5 region in the 5'LTR, and the U3R region cloned in the 3'LTR exhibited potent promoter activity. MSRV clones define a novel family of endogenous elements, HERV-W. From our data, HERV-W RNAs are copackaged in extracellular particles which might be produced by replication-competent or transcomplemented HERV-W copies or by an exogenous member of the HERV-W family.

L3 ANSWER 10 OF 37 MEDLINE
1999099005 Document Number: 99099005. PubMed ID: 9882319. Molecular

characterization and placental expression of HERV-W, a new human endogenous retrovirus family. Blond J L; Beseme F; Duret L; Bouton O; Bedin F; Perron H; Mandrand B; Mallet F. (Unite Mixte 103 CNRS-bioMerieux, Ecole Normale Superieure de Lyon, 69364 Lyon, Cedex 07, France.) JOURNAL OF VIROLOGY, (1999 Feb) 73 (2) 1175-85. Journal code: 0113724. ISSN: 0022-538X. Pub. country: United States. Language: English.

AB The multiple sclerosis-associated retrovirus (MSRV) isolated from plasma of MS patients was found to be phylogenetically and experimentally related to human endogenous retroviruses (HERVs). To characterize the MSRV-related HERV family and to test the hypothesis of a replication-competent HERV, we have investigated the expression of MSRV-related sequences in healthy tissues. The expression of MSRV-related transcripts restricted to the placenta led to the isolation of overlapping cDNA clones from a cDNA library. These cDNAs spanned a 7.6-kb region containing gag, pol, and env genes; RU5 and U3R flanking sequences; a polypurine tract; and a primer binding site (PBS). As this PBS showed similarity to avian retrovirus PBSs used by tRNATrp, this new HERV family was named HERV-W. Several genomic elements were identified, one of them containing a complete HERV-W unit, spanning all cDNA clones. Elements of this multicopy family were not replication competent, as gag and pol open reading frames (ORFs) were interrupted by frameshifts and stop codons. A complete ORF putatively coding for an envelope protein was found both on the HERV-W DNA prototype and within an RU5-env-U3R polyadenylated cDNA clone. Placental expression of 8-, 3.1-, and 1.3-kb transcripts was observed, and a putative splicing strategy was described. The apparently tissue-restricted HERV-W long terminal repeat expression is discussed with respect to physiological and pathological contexts.

L3 ANSWER 16 OF 37 MEDLINE

1998095013 Document Number: 98095013. PubMed ID: 9433428. Detection of virion-associated MSRV-RNA in serum of patients with multiple sclerosis. Garson J A; Tuke P W; Giraud P; Paranhos-Baccala G; Perron H. LANCET, (1998 Jan 3) 351 (9095) 33. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.

L3 ANSWER 18 OF 37 MEDLINE

1998005317 Document Number: 98005317. PubMed ID: 9345457. Expression of endogenous retroviruses in blood mononuclear cells and brain tissue from multiple sclerosis patients. Rasmussen H B; Geny C; Deforges L; Perron H; Tourtelotte W; Heltberg A; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) MULTIPLE SCLEROSIS, (1995 Jun) 1 (2) 82-7. Journal code: 9509185. ISSN: 1352-4585. Pub. country: ENGLAND: United Kingdom. Language: English.

AB The aim of the present study was to examine whether there is an abnormal expression of certain endogenous retroviruses in MS patients. For this purpose samples of peripheral blood mononuclear cells were obtained from 22 MS patients, a corresponding number of age and sex-matched healthy donors and five patients with other diseases affecting the central nervous system. In addition, brain specimens of macroscopic normal white and gray matter from four MS patients and a similar number of controls were included in the study. Using an enzymatic amplification technique, we found expression of the endogenous retroviral sequences, HRES-1, HERV-K10 and ERV3 in most samples of peripheral blood mononuclear cells from MS patients and controls without obvious differences between these two groups. In contrast, composite transcripts of ERV3 and a zinc finger sequence were more frequently detected in healthy donors than in MS patients. At present, the possible significance of this is uncertain. The retroviral element 4-1 was not transcribed or only transcribed at a very low level in peripheral blood cells of controls and MS patients. Transcripts of various endogenous retroviruses were also detected in the brain samples, but a different pattern was not apparent in the MS group as

compared with controls. Aspects concerning a possible association between endogenous retroviruses and autoimmunity are considered.

L3 ANSWER 20 OF 37 MEDLINE
97352842 Document Number: 97352842. PubMed ID: 9207135. Molecular identification of a novel retrovirus repeatedly isolated from patients with multiple sclerosis. The Collaborative Research Group on Multiple Sclerosis. Perron H; Garson J A; Bedin F; Beseme F; Paranhos-Baccala G; Komurian-Pradel F; Mallet F; Tuke P W; Voisset C; Blond J L; Lalande B; Seigneurin J M; Mandrand B. (bioMerieux SA, Unite Mixte de Recherche 103, Centre National de la Recherche Scientifique-bioMerieux, 46, Allee d'Italie, 69364 Lyon Cedex 07, France.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1997 Jul 8) 94 (14) 7583-8. Journal code: 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.
AB The partial molecular characterization of multiple sclerosis (MS)-associated retrovirus (MSRV), a novel retrovirus previously called LM7, is reported. MSRV has been isolated repeatedly from leptomeningeal, choroid plexus and from Epstein-Barr virus-immortalized B cells of MS patients. A strategy based on reverse transcriptase PCR with RNA-purified extracellular virions yielded an initial pol fragment from which other regions of the retroviral genome were subsequently obtained by sequence extension. MSRV-specific PCR primers amplified a pol region from RNA present at the peak of reverse transcriptase activity, coinciding with extracellular viral particles in sucrose density gradients. The same sequence was detected in noncellular RNA from MS patient plasma and in cerebrospinal fluid from untreated MS patients. MSRV is related to, but distinct from, the endogenous retroviral sequence ERV9. Whether MSRV represents an exogenous retrovirus with closely related endogenous elements or a replication-competent, virion-producing, endogenous provirus is as yet unknown. Further molecular epidemiological studies are required to determine precisely the apparent association of virions containing MSRV RNA with MS.

L3 ANSWER 21 OF 37 MEDLINE
97317644 Document Number: 97317644. PubMed ID: 9174639. Expression of endogenous retroviruses in blood mononuclear cells and brain tissue from multiple sclerosis patients. Rasmussen H B; Geny C; Deforges L; Perron H; Tourtelotte W; Heltberg A; Clausen J. (Institute of Life Sciences and Chemistry, Roskilde University, Denmark.) ACTA NEUROLOGICA SCANDINAVICA. SUPPLEMENTUM, (1997) 169 38-44. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.
AB OBJECTIVES: To compare the expression of endogenous retroviruses in MS patients and controls. MATERIAL AND METHODS: Peripheral blood mononuclear cells were obtained from 22 MS patients, a corresponding number of matched healthy donors and five patients with other central nervous system disease. Also brain specimens from MS patients and controls were obtained. Transcripts of various endogenous retroviruses in these samples were detected by RNA-PCR. RESULTS: Several endogenous retroviral sequences were transcribed in peripheral blood mononuclear cells and brain tissue from MS patients as well as controls. A composite transcript of an endogenous retrovirus and a zinc finger sequence was more frequently found in healthy donors than in MS patients. CONCLUSION: Some endogenous retroviruses are normally transcribed in white blood cells and brain tissue. The significance of those findings, which concerned the composite transcripts of the zinc finger sequence and its associated endogenous retrovirus is uncertain.

L3 ANSWER 22 OF 37 MEDLINE
97317642 Document Number: 97317642. PubMed ID: 9174637. Cell cultures and associated retroviruses in multiple sclerosis. Collaborative Research

Group on MS. Perron H; Firouzi R; Tuke P; Garson J A; Michel M; Beseme F; Bedin F; Mallet F; Marcel E; Seigneurin J M; Mandrand B. (BioMerieux S.A., UMR 103 CNRS-bioMerieux, Lyon, France.) ACTA NEUROLOGICA SCANDINAVICA. SUPPLEMENTUM, (1997) 169 22-31. Journal code: 0370337. ISSN: 0065-1427. Pub. country: Denmark. Language: English.

AB Retroviral particles associated with reverse transcriptase (RT) activity in cell-cultures from MS patients have been reported by different groups. Cell-cultures have been used for the study and characterization of the corresponding retroviral genome which we have shown is related to ERV9 in the pol region. Previously unpublished details of a study with monocyte cultures are presented together with observations on leptomeningeal and choroid-plexus cultures. The generation of self-transformed cultures after inhibition of interferon, followed by the loss of retroviral expression and recurrent apoptosis, is analyzed. Retroviral particles with RT-activity are produced in monocyte cultures with an apparent correlation with MS disease activity. However, though leptomeningeal and choroid plexus cells from MS can be passaged for a limited period, their evolution in vitro is not compatible with stable retroviral expression. These culture limitations greatly hampered progress on the elucidation of the retroviral genome sequence.

L3 ANSWER 33 OF 37 MEDLINE

93126664 Document Number: 93126664. PubMed ID: 1282730. In vitro transmission and antigenicity of a retrovirus isolated from a multiple sclerosis patient. Perron H; Gratacap B; Lalande B; Genoulaz O; Laurent A; Geny C; Mallaret M; Innocenti P; Schuller E; Stoebner P; +. (UMR 103 CNRS/BioMerieux, Ecole Normale Superieure de Lyon, France.) RESEARCH IN VIROLOGY, (1992 Sep-Oct) 143 (5) 337-50. Journal code: 8907469. ISSN: 0923-2516. Pub. country: France. Language: English.

AB We have recently isolated an apparently novel retrovirus (LM7) from a patient with multiple sclerosis (MS). We present here results showing that (1) LM7 retrovirus can be transmitted in vitro to a normal human leptomeningeal cell culture and that (2) specific antibody against this retroviral strain can be detected in MS cases. Our results suggest that, if this virus is an endogenous retrovirus, it is different from human endogenous elements already described.

L3 ANSWER 34 OF 37 MEDLINE

92170284 Document Number: 92170284. PubMed ID: 1724334. Antibody to reverse transcriptase of human retroviruses in multiple sclerosis. Perron H; Geny C; Genoulaz O; Pellat J; Perret J; Seigneurin J M. (Department of Virology, University Hospital, Grenoble, France.) ACTA NEUROLOGICA SCANDINAVICA, (1991 Dec) 84 (6) 507-13. Journal code: 0370336. ISSN: 0001-6314. Pub. country: Denmark. Language: English.

AB HTLV-1, HIV-1 and HIV-2 western blot analysis of sera from patients with multiple sclerosis (MS), from patients with other neurological diseases and from blood donors, revealed a rather frequent cross-reactivity with retroviral proteins in the MS group, though no patient was positive with the corresponding specific ELISA serology. Statistical analysis revealed a significant difference between the MS group and the two control groups for HIV-1 and HIV-2 reverse transcriptase fragments and for HTLV-1 p24. The general significance of these observations is discussed in the light of a retroviral hypothesis for the aetiology of MS. It is suggested that, if a retrovirus is present in MS patients, it does not necessarily belong to the HTLV sub-family and could as well be a lentivirus, like Visna virus, the causative agent of a demyelinating disease in sheep which is one--natural--model for MS.

L3 ANSWER 35 OF 37 MEDLINE

91194476 Document Number: 91194476. PubMed ID: 1707471. Isolation of retrovirus from patients with multiple sclerosis. Perron H;

Lalande B; Gratacap B; Laurent A; Genoulaz O; Geny C; Mallaret M; Schuller E; Stoebner P; Seigneurin J M. LANCET, (1991 Apr 6) 337 (8745) 862-3. Journal code: 2985213R. ISSN: 0140-6736. Pub. country: ENGLAND: United Kingdom. Language: English.